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=> fil hcaplu
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FILE LAST UPDATED: 10 Oct 2002  (20021010/ED)

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information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> d stat que
L11           7 SEA FILE=REGISTRY ("HUMAN IMMUNODEFICIENCY VIRUS-1 DERIVED
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                  PROTEIN-1 (RICE CLONE TBPOS-1 HOMOLOG REDUCED)"/CN)
L12           1 SEA FILE=REGISTRY "GLYCOPROTEIN 120ENV (HUMAN IMMUNODEFICIENCY
                  VIRUS 1 STRAIN RF V3 LOOP FRAGMENT)"/CN
L15         447 SEA FILE=REGISTRY GP120?/CN
L16       30872 SEA FILE=HCAPLUS L11 OR HIV1 OR HUMAN(W)IMMUNODEFICIENCY(W)VIRU
                  S1 OR (HIV OR HUMAN(W)IMMUNODEFICIENCY(W)VIRUS)(W)1
L17        4914 SEA FILE=HCAPLUS L12 OR L15 OR GP120 OR GLYCOPROTEIN120
L18          10 SEA FILE=HCAPLUS L16 AND L17 AND PRIMATE?(W)LENTIVIRUS


=> d ibib abs hitrn l18 1-10

L18  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2001:100432  HCAPLUS
DOCUMENT NUMBER:          134:277705
TITLE:                    Conservation of human immunodeficiency virus type 1
                          gp120 inner-domain sequences in lentivirus and
                          type A and B retrovirus envelope surface glycoproteins
AUTHOR(S):                Hotzel, Isidro; Cheevers, William P.
CORPORATE SOURCE:         Department of Veterinary Microbiology and Pathology,
                          Washington State University, Pullman, WA, 99164-7040,
                          USA
SOURCE:                   Journal of Virology (2001), 75(4), 2014-2018
```

CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We recently described a sequence similarity between the small ruminant lentivirus surface unit glycoprotein (SU) gp135 and the second conserved region (C2) of the **primate lentivirus gp120** which indicates a structural similarity between gp135 and the inner proximal domain of the human immunodeficiency virus type 1 gp 120. Here we found that the seven-amino-acid sequence of the **gp120** strand .beta.25 in the C5 region, which is also part of the inner proximal domain, was conserved in the SU of all lentiviruses in similar or identical positions relative to the carboxy terminus of SU. Sequences conforming to the gp135-**gp120** consensus for .beta.-strand 5 in the C2 region, which is antiparallel to .beta.25, were then sought in the SU of other lentiviruses and retroviruses. Except for the feline immunodeficiency virus, sequences similar to the **gp120**-gp135 consensus for .beta.5 and part of the preceding strand .beta.4 were present in the SU of all lentiviruses. This motif was highly conserved among strains of each lentivirus and included a strictly conserved cysteine residue in .beta.4. In addn., the .beta.4/.beta.5 consensus motif was also present in the conserved carboxy-terminal region of all type A and B retroviral envelope surface glycoproteins analyzed. Thus, the antiparallel .beta.-strands 5 and 25 of **gp120** form an SU surface highly conserved among the lentiviruses and at least partially conserved in the type A and B retroviral envelope glycoproteins.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:635843 HCAPLUS
DOCUMENT NUMBER: 133:346832

TITLE: Sequence similarity between the envelope surface unit (SU) glycoproteins of primate and small ruminant lentiviruses

AUTHOR(S): Hotzel, I.; Cheevers, W. P.
CORPORATE SOURCE: Department of Veterinary Microbiology and Pathology, Washington State University, Pullman, WA, 99164-7040, USA

SOURCE: Virus Research (2000), 69(1), 47-54
CODEN: VIREDF; ISSN: 0168-1702
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Sequence similarity has been previously described in the transmembrane domain unit of envelope glycoproteins of primate and non-primate lentiviruses but similarity between the surface unit (SU) glycoprotein of these viruses is less clear or absent. Here we describe a consistent and significant sequence-similarity between the ovine/caprine lentivirus surface glycoprotein gp135 and the **primate lentivirus gp120** in the region between variable loops V2 and V3. The biol. relevance of this sequence similarity was indicated by clustering of conserved motifs in regions of structural importance in the human immunodeficiency virus type 1 **gp120**, conservation of cysteine

residue pairs forming disulfide bonds and similar patterns of sequence variation in gp135 and **gp120** between strains. The results indicate that SU glycoproteins from primate and small ruminant lentiviruses have structurally related domains.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:325966 HCAPLUS
DOCUMENT NUMBER: 130:351221
TITLE: Stabilized **primate lentivirus** envelope glycoproteins
INVENTOR(S): Sodroski, Joseph G.; Wyatt, Richard T.; Kwong, Peter D.; Hendrickson, Wayne A.; Farzan, Michael
PATENT ASSIGNEE(S): Dana-Farber Cancer Institute, USA; The Trustees of Columbia University in the City of New York
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924465	A1	19990520	WO 1998-US24001	19981110
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
WO 9924553	A2	19990520	WO 1998-US23905	19981110
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 9924065	A1	19990520	WO 1998-US23906	19981110
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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AU 9913963	A1	19990531	AU 1999-13963	19981110
AU 9914545	A1	19990531	AU 1999-14545	19981110
EP 1037963	A1	20000927	EP 1998-959406	19981110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-966932 A 19971110

US	1997-966987	A	19971110
US	1997-967148	A	19971110
US	1997-967403	A	19971110
US	1997-967708	A	19971110
US	1997-976741	A	19971124
US	1998-89580P	P	19980617
US	1998-89581P	P	19980617
US	1998-100521	A	19980618
US	1998-100529	A	19980618
US	1998-100631	A	19980618
US	1998-100762	A	19980618
US	1998-100763	A	19980618
US	1998-100764	A	19980618
WO	1998-US23905	W	19981110
WO	1998-US23906	W	19981110
WO	1998-US24001	W	19981110

AB A modified polypeptide corresponding to an envelope glycoprotein of a **primate lentivirus** is described. The polypeptide has been modified from the wild-type structure so that it has cysteine amino acid residues introduced to create disulfide bonds, a cavity is filled with hydrophobic amino acids, a Pro residue is introduced at a defined turn structure of the protein, or the hydrophobicity is increased across the interface between different domains, while retaining the overall 3-dimensional structure of a discontinuous conserved epitope of the wild-type protein. Preferably, the polypeptide has more than one of those characteristics. Preferably, the **primate lentivirus** is HIV, and the protein is **HIV-1 gp120**.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2002 ACS

Inventor search Wya

ACCESSION NUMBER: 1999:325965 HCAPLUS
DOCUMENT NUMBER: 130:351220
TITLE: Glycosylated modified **primate lentivirus** envelope polypeptides
INVENTOR(S): Wyatt, Richard T.; Sodroski, Joseph G.; Kwong, Peter D.; Hendrickson, Wayne A.
PATENT ASSIGNEE(S): Dana-Farber Cancer Institute, USA; The Trustees of Columbia University in the City of New York
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924464	A1	19990520	WO 1998-US23998	19981110
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
WO 9924065	A1	19990520	WO 1998-US23906	19981110
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				

DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9913962	A1	19990531	AU 1999-13962	19981110
AU 9914545	A1	19990531	AU 1999-14545	19981110
EP 1037963	A1	20000927	EP 1998-959406	19981110

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

PRIORITY APPLN. INFO.:	US 1997-966932	A	19971110
	US 1997-966987	A	19971110
	US 1997-967403	A	19971110
	US 1997-967708	A	19971110
	US 1997-976148	A	19971110
	US 1997-976741	A	19971124
	US 1998-89580P	P	19980617
	US 1998-89581P	P	19980617
	US 1998-100521	A	19980618
	US 1998-100529	A	19980618
	US 1998-100631	A	19980618
	US 1998-100762	A	19980618
	US 1998-100763	A	19980618
	US 1998-100764	A	19980618
	US 1997-967148	A	19971110
	WO 1998-US23905	W	19981110
	WO 1998-US23906	W	19981110
	WO 1998-US23998	W	19981110

AB A modified polypeptide corresponding to an envelope glycoprotein of a **primate lentivirus** is described. The polypeptide has been modified from the wild-type structure so that it has at least two of the glycosylation sites proximal to the CD4 binding site or chemokine receptor site altered so that the alteration prevents glycosylation at that site or where glycosylation sites distal to these sites have been derivatized with a mol. adjuvant, while retaining the overall 3-dimensional structure of a discontinuous conserved epitope of the wild-type protein. Preferably, the polypeptide has both changes. Preferably, the **primate lentivirus** is HIV, and the protein is HXBc2 strain **HIV-1** gp 120.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1999:271509 HCAPLUS
DOCUMENT NUMBER:	130:292443
TITLE:	Recombinant, non-infective retrovirus having high expression of immunogenic antigens
INVENTOR(S):	Lu, Yichen; Touzjian, Neal; Auewarakul, Prasert; Bharmarapravati, Natth
PATENT ASSIGNEE(S):	Institute for Vaccine Development, USA; Avant Immunotherapeutics, Inc.
SOURCE:	PCT Int. Appl., 52 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9919501	A1	19990422	WO 1998-US21739	19981014
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9910872	A1	19990503	AU 1999-10872	19981014

PRIORITY APPLN. INFO.: US 1997-61894P P 19971014
WO 1998-US21739 W 19981014

AB Provided is a recombinant provirus (preferably a **primate lentivirus** such as HTLV or HIV) that disrupts the first half of the viral replication cycle while mimicking the second half, thereby permitting prodn. of sol. antigens such as **gp120**, p55, and p24. This recombinant provirus preferably contains two independent sets of deletion mutations to abolish the infectivity of the virus. One such mutation results in the inactivation of the reverse transcriptase and/or integrase genes from the virus, both of which play essential roles in the first half of the viral replication cycle. The other mutation involves deletion of the 3' long terminal repeat element (LTR) and the substitution of a heterologous poly A at the 3' end, whereby efficient expression of viral genes and formation of virus particles can still occur, yet the virus is unable to successfully replicate upon entering the cell or integrate into the host cell's chromosome. Thus, the invention provides a DNA sequence corresponding to a retroviral genome wherein the 3' LTR has been replaced by a heterologous poly A sequence, and wherein the genome is int- and/or RT-. This recombinant retrovirus can be used to transform an animal cell line to produce secreted viral antigens, which can be used as immunogens.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:191187 HCAPLUS
DOCUMENT NUMBER: 131:41932
TITLE: Characterization of a neutralization-escape variant of SHIVKU-1, a virus that causes acquired immune deficiency syndrome in pig-tailed macaques
AUTHOR(S): Narayan, Shanil V.; Mukherjee, Sampa; Jia, Fenglan; Li, Zhuang; Wang, Chunyang; Foresman, Larry; McCormick-Davis, Coleen; Stephens, Edward B.; Joag, Sanjay V.; Narayan, Opendra
CORPORATE SOURCE: Dep. Microbiol. Mol. Genet. Immunol., Univ. Kansas Medical Center, Kansas City, KS, 66160-7420, USA

SOURCE: Virology (1999), 256(1), 54-63
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A chimeric simian-human immunodeficiency virus (SHIV-4) contg. the tat, rev, vpu, and env genes of HIV type 1 (**HIV-1**) in a genetic background of SIVmac239 was used to develop an animal model in which a **primate lentivirus** expressing the **HIV -1** envelope glycoprotein caused acquired immune deficiency syndrome (AIDS) in macaques. An SHIV-infected pig-tailed macaque that died from AIDS at 24 wk postinoculation experienced 2 waves of viremia: one extending from wk 2-8 and the 2nd extending from wk 18 until death. Virus (SHIVKU-1) isolated during the 1st wave was neutralized by antibodies appearing at the end of the 1st viremic phase, but the virus (SHIVKU-1b) isolated during the 2nd viremic phase was not neutralized by these antibodies. Inoculation of SHIVKU-1b into 4 pig-tailed macaques resulted in severe CD4+ T cell loss by 2 wk postinoculation, and all 4 macaques died from AIDS at 23-34 wk postinoculation. Because this virus had a neutralization-resistant phenotype, the env gene was sequenced and these sequences compared with those of the env gene of SHIVKU-1 and parental SHIV-4. With ref. to SHIV-4, SHIVKU-1b had 18 and 6 consensus amino acid substitutions in the **gp120** and gp41 regions of Env, resp. These compared with 10 and 3 amino acid substitutions in the **gp120** and gp41 regions of SHIVKU-1. Our data suggested that SHIVKU-1 and SHIVKU-1b probably evolved from a common ancestor but that SHIVKU-1b did not evolve from SHIVKU-1. A chimeric virus, SHIVKU-1bMC17, constructed with the consensus env from the SHIVKU-1b on a background of SHIV-4, confirmed that amino acid substitutions in Env were responsible for the neutralization-resistant phenotype. These results are consistent with the hypothesis that neutralizing antibodies induced by SHIVKU-1 in pig-tailed macaque resulted in the selection of a neutralization-resistant virus that was responsible for the 2nd wave of viremia. (c) 1999 Academic Press.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:73608 HCAPLUS
DOCUMENT NUMBER: 130:266247

TITLE: Neutralizing antibody directed against the **HIV -1** envelope glycoprotein can completely block **HIV-1**/SIV chimeric virus infections of macaque monkeys

AUTHOR(S): Shibata, Riri; Igarash, Tatsuhiko; Haigwood, Nancy; Buckler-White, Alicia; Ogert, Robert; Ross, William; Willey, Ronald; Cho, Michael W.; Martin, Malcolm A.
CORPORATE SOURCE: Lab. Mol. Microbiology, National Inst. Health, Bethesda, MD, 20892, USA

SOURCE: Nature Medicine (New York) (1999), 5(2), 204-210
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Virus-specific antibodies protect individuals against a wide variety of viral infections. To assess whether human immunodeficiency virus type 1 (**HIV-1**) envelope-specific antibodies confer resistance against **primate lentivirus** infections, we purified IgG from chimpanzees infected with several different **HIV-1** isolates, and used this for passive immunization of pig-tailed macaques. These monkeys were subsequently challenged i.v. with a chimeric simian-human immunodeficiency virus (SHIV) bearing an envelope glycoprotein derived from HIV-1OH12, a dual-tropic primary virus isolate. Here we show that anti-SHIV neutralizing activity, detd. in vitro using an assay measuring loss of infectivity, is the abs. requirement for antibody-mediated protection in vivo. Using an assay that measures 100% neutralization, the titer in plasma for complete protection of the SHIV-challenge macaques was in the range of 1:5-1:8. The **HIV-1**-specific neutralizing antibodies studied are able to bind to native gp 120 present on infectious virus particles. Administration of non-neutralizing anti-HIV IgG neither inhibited nor enhanced a subsequent SHIV infection.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:810759 HCAPLUS
DOCUMENT NUMBER: 130:163810
TITLE: "Hidden" dUTPase sequence in human immunodeficiency virus type 1 **gp120**
AUTHOR(S): Abergel, Chantal; Robertson, David L.; Claverie, Jean-Michel
CORPORATE SOURCE: Laboratory of Structural and Genetic Information, CNRS EP-91, Marseille, F-13402, Fr.
SOURCE: Journal of Virology (1999), 73(1), 751-753
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A coding region homologous to the sequence for essential eukaryotic enzyme dUTPase has been identified in different genomic regions of several viral lineages. Unlike the nonprimate lentiviruses (caprine arthritis-encephalitis virus, equine infections anemia virus, feline immunodeficiency virus, and visna virus), where dUTPase is integrated into the pol coding region, this enzyme has never been demonstrated to be present in the **primate lentivirus** genomes (human immunodeficiency virus type 1 [**HIV-1**], HIV-2, or the related simian immunodeficiency virus). A novel approach allowed us to identify a weak but significant sequence similarity between **HIV-1 gp120** and the human dUTPase. This finding was then extended to all of the **primate lentivirus** lineages. Together with the recently reported fragmentary structural similarity between the V3 loop region and the Escherichia coli dUTPase (P. D. Kwong, R. Wyatt, J. Robinson, R. W. Sweet, J. Sodroski, and W. A. Hendrickson, Nature 393:648-659, 1998), our results strongly suggest that an ancestral dUTPase gene has evolved into the present **primate lentivirus** CD4 and cytokine receptor interacting region of **gp120**.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:558067 HCAPLUS
DOCUMENT NUMBER: 119:158067
TITLE: Rates of amino acid change in the envelope protein correlate with pathogenicity of primate lentiviruses
AUTHOR(S): Shpaer, Eugene G.; Mullins, James I.
CORPORATE SOURCE: Sch. Med., Stanford Univ., Stanford, CA, 94305-5402, USA
SOURCE: Journal of Molecular Evolution (1993), 37(1), 57-65
CODEN: JMEVAU; ISSN: 0022-2844
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A spectrum of pathogenicity has been obsd. for primate lentiviruses in their natural hosts. For example, human immunodeficiency virus type 1 (**HIV-1**) is a potent etiol. agent for AIDS in man, whereas there is no evidence to date which indicates that simian immunodeficiency virus from African green monkeys (SIVAGM) causes immunodeficiency in AGM. The authors measured the relative rates of amino acid change, as the ratio of the no. of nonsynonymous to synonymous (silent) nucleotide substitutions, for 6 primate lentiviruses evolving in their resp. hosts. These rates for the external envelope glycoprotein (**gp120**) and gag coding sequences are 2-3 times higher for pathogenic **HIV-1** and SIVmac (macaque) than for minimally pathogenic SIVAGM and SIVsmm (sooty mangabey), and intermediate for HIV-2. The authors speculate that the increased rates of nonsynonymous changes in **gp120** and gag coding sequences are due to viral escape from immune surveillance and are indicative of higher immunogenicity of these proteins in their hosts. Based on these results and available exptl. data, the authors conclude that there is a pos. correlation between lentiviral pathogenicity and immunogenicity of the Env and Gag proteins in a given host. This hypothesis is consistent with recent data suggesting that immune system activation or autoimmunity induced by viral antigens may be important in the pathogenesis of AIDS.

L18 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:512051 HCAPLUS
DOCUMENT NUMBER: 113:112051
TITLE: An African **primate lentivirus** (SIVsm) closely related to HIV-2
AUTHOR(S): Hirsch, Vanessa M.; Olmsted, Robert A.; Murphey-Corb, Michael; Purcell, Robert H.; Johnson, Philip R.
CORPORATE SOURCE: Dep. Microbiol., Georgetown Univ., Rockville, MD, 20852, USA
SOURCE: Nature (London) (1989), 339(6223), 389-92
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ancestors of the human immunodeficiency viruses (**HIV-1** and HIV-2) may have evolved from a reservoir of African nonhuman primate lentiviruses, termed simian immunodeficiency viruses (SIV). None of the SIV strains characterized so far are closely related to **HIV**

-1. HIV-2, however, is closely related to SIV (SIVmac) isolated from captive rhesus macaques (Macaca mulatta). SIV infection of feral Asian macaques has not been demonstrated by serol. surveys. Thus, macaques may have acquired SIV in captivity by cross-species transmission from an SIV-infected African primate. Sooty mangabeys (Cercocebus atys), an African primate species indigenous to West Africa, however, are infected with SIV (SIVsm) both in captivity and in the wild (P. Fultz, personal communication). SIVsm was cloned and sequenced, and was found to be closely related to SIVmac and HIV-2. These results suggest that SIVsm has infected macaques in captivity and humans in West Africa and evolved as SIVmac and HIV-2, resp.

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=> d stat que
L11           7 SEA FILE=REGISTRY ("HUMAN IMMUNODEFICIENCY VIRUS-1 DERIVED
                PEPTIDE"/CN OR "HUMAN IMMUNODEFICIENCY VIRUS-1 TAT BINDING
                PROTEIN-1 (RICE CLONE TBPOS-1 HOMOLOG REDUCED)"/CN)
L12           1 SEA FILE=REGISTRY "GLYCOPROTEIN 120ENV (HUMAN IMMUNODEFICIENCY
                VIRUS 1 STRAIN RF V3 LOOP FRAGMENT)"/CN
L13           4 SEA FILE=REGISTRY (CD4/CN OR "CD4 (ANTIGEN) (DELPHINAPTERUS
                LEUCAS THYMUS PRECURSOR)"/CN OR "CD4 (ANTIGEN) (GALLUS
                DOMESTICUS CLONE P2.6 GENE CD4 PRECURSOR)"/CN OR "CD4 (ANTIGEN)
                 (HUMAN CLONE CD4-IGG2HC-PRCCMV N-TERMINAL FRAGMENT) FUSION
                PROTEIN WITH IMMUNOGLOBULIN G2, ANTI-(HUMAN IMMUNODEFICIENCY
                VIRUS ENVELOPE PROTEIN GP120ENV) (HUMAN .GAMMA.2-CHAIN
                FRAGMENT)"/CN)
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L15         447 SEA FILE=REGISTRY GP120?/CN
L16       30872 SEA FILE=HCAPLUS L11 OR HIV1 OR HUMAN(W)IMMUNODEFICIENCY(W)VIRU
                S1 OR (HIV OR HUMAN(W)IMMUNODEFICIENCY(W)VIRUS)(W)1
L17        4914 SEA FILE=HCAPLUS L12 OR L15 OR GP120 OR GLYCOPROTEIN120
L18          10 SEA FILE=HCAPLUS L16 AND L17 AND PRIMATE?(W)LENTIVIRUS
L19       34977 SEA FILE=HCAPLUS L13 OR CD4 OR CD(W)4
L20        6408 SEA FILE=HCAPLUS L14 OR CYTOKINE (W)RECEPTOR?
L21        1631 SEA FILE=HCAPLUS L16 AND L17 AND (L19 OR L20)
L22          62 SEA FILE=HCAPLUS L21 (L) GLYCOSYLATION
L23           9 SEA FILE=HCAPLUS L22 AND MODIFICATION
L24           8 SEA FILE=HCAPLUS L23 NOT L18

=> d ibib abs hitrn l24 1-8

L24  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2001:205198  HCAPLUS
DOCUMENT NUMBER:          134:352174
TITLE:                    Loss of a single N-linked glycan allows CD4
                          -independent human immunodeficiency virus type 1
                          infection by altering the position of the
                          gp120 V1/V2 variable loops
AUTHOR(S):                Kolchinsky, Peter; Kiprilov, Enko; Bartley, Peter;
                          Rubinstein, Roee; Sodroski, Joseph
CORPORATE SOURCE:         Department of Cancer Immunology and AIDS, Dana-Farber
                          Cancer Institute, Harvard Medical School, Boston, MA,
                          02115, USA
```

SOURCE: Journal of Virology (2001), 75(7), 3435-3443
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **gp120** envelope glycoprotein of primary human immunodeficiency virus type 1 (**HIV-1**) promotes virus entry by sequentially binding **CD4** and the CCR5 chemokine receptor on the target cell. Previously, we adapted a primary **HIV-1** isolate, ADA, to replicate in **CD4**-neg. canine cells expressing human CCR5. The **gp120** changes responsible for **CD4**-independent replication were limited to the V2 loop-V1/V2 stem. Here we show that elimination of a single **glycosylation** site at asparagine 197 in the V1/V2 stem is sufficient for **CD4**-independent **gp120** binding to CCR5 and for **HIV-1** entry into **CD4**-neg. cells expressing CCR5. Deletion of the V1/V2 loops also allowed **CD4**-independent viral entry and **gp120** binding to CCR5. The binding of the wild-type ADA **gp120** to CCR5 was less dependent upon **CD4** at 4.degree.C than at 37.degree.C. In the absence of the V1/V2 loops, neither removal of the N-linked carbohydrate at asparagine 197 nor lowering of the temp. increased the **CD4**-independent phenotypes. A CCR5-binding conformation of **gp120**, achieved by **CD4** interaction or by **modification** of temp., **glycosylation**, or variable loops, was preferentially recognized by the monoclonal antibody 48d. These results suggest that the CCR5-binding region of **gp120** is occluded by the V1/V2 variable loops, the position of which can be modulated by temp., **CD4** binding, or an N-linked glycan in the V1/V2 stem.

REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:204209 HCAPLUS
DOCUMENT NUMBER: 130:351112

TITLE: Tyrosine sulfation of the amino terminus of CCR5 facilitates **HIV-1** entry

AUTHOR(S): Farzan, Michael; Mirzabekov, Tajib; Kolchinsky, Peter; Wyatt, Richard; Cayabyab, Mark; Gerard, Norma P.; Gerard, Craig; Sodroski, Joseph; Choe, Hyeryun
CORPORATE SOURCE: Division of Human Retrovirology Dana-Farber Cancer Institute Department of Pathology, Harvard Medical School, Boston, MA, 02115, USA

SOURCE: Cell (Cambridge, Massachusetts) (1999), 96(5), 667-676
CODEN: CELLB5; ISSN: 0092-8674
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chemokine receptors and related seven-transmembrane-segment (7TMS) receptors serve as coreceptors for entry of human and simian immunodeficiency viruses (**HIV-1**, HIV-2, and SIV) into target cells. Each of these otherwise diverse coreceptors contains an N-terminal region that is acidic and tyrosine rich. Here, we show that the chemokine receptor CCR5, a principal **HIV-1**

coreceptor, is posttranslationally modified by O-linked **glycosylation** and by sulfation of its N-terminal tyrosines. Sulfated tyrosines contribute to the binding of CCR5 to MIP-1.alpha., MIP-1.beta., and **HIV-1 gp120/CD4** complexes and to the ability of **HIV-1** to enter cells expressing CCR5 and **CD4**. CXCR4, another important **HIV-1** coreceptor, is also sulfated. Tyrosine sulfation may contribute to the natural function of many 7TMS receptors and may be a **modification** common to primate immunodeficiency virus coreceptors.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:172289 HCAPLUS

DOCUMENT NUMBER: 130:293013

TITLE: Probability analysis of variational crystallization and its application to **gp120**, the exterior envelope glycoprotein of type 1 human immunodeficiency virus (**HIV-1**)

AUTHOR(S): Kwong, Peter D.; Wyatt, Richard; Desjardins, Elizabeth; Robinson, James; Culp, Jeffrey S.; Hellmig, Brian D.; Sweet, Raymond W.; Sodroski, Joseph; Hendrickson, Wayne A.

CORPORATE SOURCE: Department of Biochemistry and Molecular Biophysics, Columbia University, New York, NY, 10032, USA

SOURCE: Journal of Biological Chemistry (1999), 274(7), 4115-4123
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The extensive **glycosylation** and conformational mobility of **gp120**, the envelope glycoprotein of type 1 human immunodeficiency virus (**HIV-1**), pose formidable barriers for crystn. To surmount these difficulties, we used probability anal. to det. the most effective crystn. approach and derive equations which show that a strategy, which we term variational crystn., substantially enhances the overall probability of crystn. for **gp120**.. Variational crystn. focuses on protein **modification** as opposed to crystn. screening. Multiple variants of **gp120** were analyzed with an iterative cycle involving a limited set of crystn. conditions and biochem. feedback on protease sensitivity, **glycosylation** status, and monoclonal antibody binding. Sources of likely conformational heterogeneity such as N-linked carbohydrates, flexible or mobile N and C termini, and variable internal loops were reduced or eliminated, and ligands such as **CD4** and antigen-binding fragments (Fabs) of monoclonal antibodies were used to restrict conformational mobility as well as to alter the crystn. surface. Through successive cycles of manipulation involving 18 different variants, we succeeded in growing six different types of **gp120** crystals. One of these, a ternary complex composed of **gp120**, its receptor **CD4**, and the Fab of the human neutralizing monoclonal antibody 17b, diffracts to a min. Bragg spacing of at least 2.2 .ANG. and is suitable for structural anal.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:414450 HCAPLUS
DOCUMENT NUMBER: 127:148122
TITLE: Refocusing neutralizing antibody response by targeted dampening of an immunodominant epitope
AUTHOR(S): Garrity, Robert R.; Rimmelzwaan, Guus; Minassian, Anton; Tsai, Wen-Po; Lin, George; de Jong, Jean-Jacques; Goudsmit, Jaap; Nara, Peter L.
CORPORATE SOURCE: Laboratory of Vaccine Resistant Diseases, Division of Basic Sciences, National Institute-Frederick Cancer Research and Development Center, Frederick, MD, 21702, USA
SOURCE: Journal of Immunology (1997), 159(1), 279-289
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Immunodominant epitopes are known to suppress a primary immune response to other antigenic determinants by a no. of mechanisms. Many pathogens have used this strategy to subvert the immune response and may be a mechanism responsible for limited vaccine efficiencies. **HIV-1** vaccine efficacy appears to be complicated similarly by a limited, immunodominant, isolate-restricted immune response generally directed toward determinants in the third variable domain (V3) of the major envelope glycoprotein, **gp120**. To overcome this problem, the authors have investigated an approach based on masking the V3 domain through addn. of N-linked carbohydrate and redn. in net pos. charge. N-linked modified gp120s were expressed by recombinant vaccinia virus and used to immunize guinea pigs by infection and protein boosting. This **modification** resulted in variable site-specific **glycosylation** and antigenic dampening, without loss of **gp120/CD4** binding or virus neutralization. Most importantly, V3 epitope damping shifted the dominant type-specific neutralizing Ab response away from V3 to an epitope in the first variable domain (V1) of **gp120**. Interestingly, in the presence of V3 dampening V1 changes from an immunodominant non-neutralizing epitope to a primary neutralizing epitope with broader neutralizing properties. In addn., Ab responses were also obsd. to conserved domains in C1 and C5. These results suggest that selective epitope dampening can lead to qual. shifts in the immune response resulting in second order neutralizing responses that may prove useful in the fine manipulation of the immune response and in the development of more broadly protective vaccines and therapeutic strategies.

L24 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:495368 HCAPLUS
DOCUMENT NUMBER: 125:162898
TITLE: Differential **glycosylation**, virion incorporation, and sensitivity to neutralizing antibodies of human immunodeficiency virus type 1 envelope produced from infected primary T-lymphocyte

and macrophage cultures
AUTHOR(S): Willey, Ronald L.; Shibata, Riri; Freed, Eric O.; Cho, Michael W.; Martin, Malcolm A.
CORPORATE SOURCE: Laboratory Molecular Microbiology, National Insitute Allergy and Infectious Diseases, Bethesda, MD, 20892, USA
SOURCE: Journal of Virology (1996), 70(9), 6431-6436
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two primary cell targets for human immunodeficiency virus type 1 (**HIV-1**) infection in vivo are **CD4**+ T lymphocytes and monocyte-derived macrophages (MDM). **HIV-1** encodes envelope glycoproteins which mediate virus entry into these cells. Infected and radiolabeled primary peripheral blood mononuclear cell (PBMC) and MDM cultures were utilized to examine the biochem. and antigenic properties of the **HIV-1** envelope produced in these 2 cell types. The **gp120** produced in MDM migrates as a broad, diffuse band in SDS-PAGE compared with that of the more homogeneous **gp120** released from PBMCs. Glycosidase analyses indicated that the diffuse appearance of the MDM **gp120** is due to the presence of asparagine-linked carbohydrates contg. lactosaminoglycans, a **modification** not obsd. with the **gp120** produced in PBMCs. Neutralization expts., using isogeneic PBMC and MDM-derived macrophage-tropic **HIV-1** isolates, indicate that 8- to 10-fold more neutralizing antibody, directed against the viral envelope, is required to block virus produced from MDM. These results demonstrate that **HIV-1** released from infected PBMC and MDM cultures differs in its biochem. and antigenic properties.

L24 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:204581 HCAPLUS
DOCUMENT NUMBER: 124:255413
TITLE: Biological properties of recombinant HIV envelope synthesized in CHO **glycosylation**-mutant cell lines
AUTHOR(S): Fenouillet, Emmanuel; Miquelis, Raymond; Drillien, Robert
CORPORATE SOURCE: IFR Jean Roche, Faculte de Medecine Nord, Marseille, 13015, Fr.
SOURCE: Virology (1996), 218(1), 224-31
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB N-**glycosylation** of the human immunodeficiency virus type-1 envelope (Env) glycoprotein precursor (gp 160) occurs by transfer of Glc3Man9GlcNAc2 to the nascent protein. Maturation then occurs via cleavage of the 3 Glc residues, which starts during translation. These events are considered necessary to create Env functional conformation: treatment with .alpha.-glucosidase inhibitors, but not .alpha.-mannosidase inhibitors (i) impairs gp 160 cleavage into **gp120** and gp41-mediated membrane fusion. These inhibitors are of therapeutic

interest. Here, using a collection of parent and mutant CHO cells that possess mutations in different steps of **glycosylation**, the role of glycans in both the processing and the properties of recombinant gp160 expressed from a vaccinia virus vector is reassessed. Mutant cells were as follows: Lec23 (which lacks .alpha.-glucosidase I activity) produces a collection of triglucosylated structures (Glc3Man7-8GlcNac2); LEC10 (which has increased GlcNAc transferase III activity) produces complex glycans with a bisected GlcNAc residue; Lec1 (which lacks GlcNAc transferase I) and Lec3.2.8.1 (which lacks GlcNAc transferase I and has decreased activity of CMP-NeuNAc and UDP-Gal translocases) produce Man5GlcNac2 glycans at complex or hybrid sites. As expected, **glycosylation** of Env produced from mutants was affected but, irresp. of the **glycosylation** phenotype, (i) similar quantities of Env were synthesized, (ii) the immunoreactivity of V3 was similar, (iii) gp160 was efficiently cleaved into **gp120** and gp41, (vi) Env was exposed at the cell membrane, (v) secreted **gp120** bound **CD4**, and (vi) membrane gp41 was able to induce membrane fusion with **CD4**+ cells. Thus, the **glycosylation** alterations examd. are dispensable for Env processing and biol. activity in CHO cells. In particular, removal of the 3 outer Glc residues was not required per se for Env folding in this system because functional Env is obtained from Lec23 cells: it appears therefore that lack of **modification** is not equiv. to drug inhibition of **modification**. These data are discussed in the light or previous reports describing the use of glycosidase inhibitors to alter **glycosylation**.

L24 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:95221 HCAPLUS
DOCUMENT NUMBER: 112:95221
TITLE: **Glycosylation** and processing of the human immunodeficiency virus type 1 envelope protein
AUTHOR(S): Kozarsky, Karen; Penman, Marsha; Basiripour, Ladan; Haseltine, William; Sodroski, Joseph; Krieger, Monty
CORPORATE SOURCE: Whitaker Coll., Massachusetts Inst. Technol., Cambridge, MA, USA
SOURCE: J. Acquired Immune Defic. Syndr. (1989), 2(2), 163-9
CODEN: JAISET
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human immunodeficiency virus type 1 (**HIV-1**) envelope protein is synthesized as a gp160 precursor that is cleaved to a 120 kDa exterior glycoprotein (**gp120**) and a 41 kDa transmembrane glycoprotein (gp41). The **HIV-1** envelope protein was stably expressed under the control of the trans-activator proteins tat and rev, in wild-type and mutant Chinese hamster ovary (CHO) cells. The mutant, ldlD, is conditionally defective for the addn. of galactose and N-acetylgalactosamine to oligosaccharide chains. The effects of **glycosylation modification** on the **HIV-1** envelope's structure and function were examd. The effects of galactosylation on the structure of the envelope proteins suggest that cleavage of the gp160 precursor into **gp120** and gp41 occurs intracellularly, apparently concurrent with the addn. of galactose to N-linked oligosaccharides of the envelope proteins. No evidence for O-linked **glycosylation** of the envelope proteins in CHO cells was

obsd. The envelope protein in the transfected hamster cells mediated the fusion of these cells with **CD4**-pos. lymphocytes, and this fusogenic activity was independent of the addn. of either galactose or N-acetylgalactosamine to oligosaccharides in the transfected cells.

L24 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:110380 HCAPLUS
DOCUMENT NUMBER: 110:110380
TITLE: Model for intracellular folding of the human immunodeficiency virus type 1 **gp120**
AUTHOR(S): Fennie, Christopher; Lasky, Laurence A.
CORPORATE SOURCE: Dep. Mol. Immunol., Genetech, Inc., South San Francisco, CA, 94080, USA
SOURCE: J. Virol. (1989), 63(2), 639-46
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The intracellular folding of the human immunodeficiency virus type 1 **gp120** was assessed by analyzing the ability of the glycoprotein to bind to the viral receptor **CD4**. Pulse-chase expts. revealed that the glycoprotein was initially produced in a conformation that was unable to bind to **CD4** and that the protein attained the appropriate tertiary structure for binding with a half-life of .apprx.30 min. The protein appears to fold within the rough endoplasmic reticulum, since blocking of transport to the Golgi app. by the oxidative phosphorylation inhibitor carbonyl cyanide m-chlorophenylhydrazone did not appear to perturb the folding kinetics of the mol. The relatively lengthy folding time was not due to **modification** of the large no. of N-linked **glycosylation** sites on **gp120**, since inhibition of the first steps in oligosaccharide **modification** by the inhibitors deoxynojirimycin or deoxymannojirimycin did not impair the **CD4**-binding activity of the glycoprotein. However, prodn. of the glycoprotein in the presence of tunicamycin and removal of the N-linked sugars by endoglycosidase H treatment both resulted in deglycosylated proteins that were unable to bind to **CD4**, suggesting in agreement with previous results, that **glycosylation** contributes to the ability of **gp120** to bind to **CD4**. Interestingly, incomplete endoglycosidase H treatment revealed that a partially glycosylated glycoprotein could bind to the receptor, implying that a subset of **glycosylation** sites, perhaps some of those conserved in different isolates of human immunodeficiency virus type 1, might be important for binding of the viral glycoprotein to the **CD4** receptor.

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Li 09/446,799

Display Sets

Set Items Description
S1 163320 (HUMAN(W)IMMUNODEFICIENCY(W)VIRUS1 OR HUMAN(W)IMMUNODEFICI-
ENCY(W)VIRUS(2W)1 OR HIV1 OR HIV(W)1(S)GP120 OR GLYCOPROTEIN(-
W)120 OR (GP OR GLYCOPROTEIN)(W)120)
S2 21197 (HUMAN(W)IMMUNODEFICIENCY(W)VIRUS1 OR HUMAN(W)IMMUNODEFICI-
ENCY(W)VIRUS(2W)1 OR HIV1 OR HIV(W)1)(S)(GP120 OR GLYCOPROTEI-
N(W)120 OR (GP OR GLYCOPROTEIN)(W)120)
S3 656 (S1 OR S2) AND PRIMATE?(W)LENTIVIR?
S4 238 RD (unique items)
S5 52 S4 (S)ENVELOPE?(W)(PROTEIN? OR GLYCOPROTEIN?)
?s s5 and (cd4 or cd(w)4 or chemokine?(w)receptor?)
S6 20 S5 AND (CD4 OR CD(W)4 OR CHEMOKINE?(W)RECEPTOR?)

t6/3 ab/1-20
>>>No matching display code(s) found in file(s): 65, 342, 345

6/AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11273226 21306366 PMID: 11413331
Functional analysis of the disulfide-bonded loop/chain reversal region of human immunodeficiency virus type 1 gp41 reveals a critical role in gp120-gp41 association.
Maerz A L; Drummer H E; Wilson K A; Poumbourios P
St. Vincent's Institute of Medical Research, Fitzroy, Victoria 3065, Australia.
Journal of virology (United States) Jul 2001, 75 (14) p6635-44, ISSN 0022-538X Journal Code: 0113724
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Human immunodeficiency virus type 1 (HIV-1) entry into cells is mediated by the surface-exposed envelope protein (SU) gp120 , which binds to cellular CD4 and chemokine receptors , triggering the membrane fusion activity of the transmembrane (TM) protein gp41. The core of gp41 comprises an N-terminal triple-stranded coiled coil and an antiparallel C-terminal helical segment which is packed against the exterior of the coiled coil and is thought to correspond to a fusion-activated conformation. The available gp41 crystal structures lack the conserved disulfide-bonded loop region which, in human T-lymphotropic virus type 1 (HTLV-1) and murine leukemia virus TM proteins, mediates a chain reversal, connecting the antiparallel N- and C-terminal regions. Mutations in the HTLV-1 TM protein gp21 disulfide-bonded loop/chain reversal region adversely affected fusion activity without abolishing SU-TM association (A. L. Maerz, R. J. Center, B. E. Kemp, B. Kobe, and P. Poumbourios, J. Virol. 74:6614-6621, 2000). We now report that in contrast to our findings with HTLV-1, conservative substitutions in the HIV - 1 gp41 disulfide-bonded loop/chain reversal region abolished association with gp120 . While the mutations affecting gp120 -gp41 association also affected cell-cell fusion activity, HIV - 1 glycoprotein maturation appeared normal. The mutant glycoproteins were processed, expressed at the cell surface, and efficiently immunoprecipitated by conformation-dependent monoclonal antibodies. The gp120 association site includes aromatic and hydrophobic residues on either side of the gp41 disulfide-bonded loop and a basic residue within the loop. The HIV - 1 gp41 disulfide-bonded loop/chain reversal region is a critical gp120 contact site; therefore, it is also likely to play a central role in fusion activation by linking CD4 plus chemokine receptor -induced conformational changes in gp120 to gp41 fusogenicity. These gp120 contact residues are present in diverse primate lentiviruses , suggesting conservation of function.

6/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10201842 99189362 PMID: 10087226
Characterization of a neutralization-escape variant of SHIVKU-1, a virus that causes acquired immune deficiency syndrome in pig-tailed macaques.
Narayan S V; Mukherjee S; Jia F; Li Z; Wang C; Foresman L; McCormick-Davis C; Stephens E B; Joag S V; Narayan O
Department of Microbiology, Molecular Genetics and Immunology, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, Kansas 66160-7420, USA.

Virology (UNITED STATES) Mar 30 1999, 256 (1) p54-63, ISSN 0042-6822 Journal Code: 0110674
Contract/Grant No.: AI-38492; AI; NIAID; AI-40372; AI; NIAID; NS-32203; NS; NINDS; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A chimeric simian-human immunodeficiency virus (SHIV-4) containing the tat, rev, vpu, and env genes of HIV type 1 (HIV-1) in a genetic background of SIVmac239 was used to develop an animal model in which a primate lentivirus expressing the HIV-1 envelope glycoprotein caused acquired immune deficiency syndrome (AIDS) in macaques. An SHIV-infected pig-tailed macaque that died from AIDS at 24 weeks postinoculation experienced two waves of viremia: one extending from weeks 2-8 and the second extending from week 18 until death. Virus (SHIVKU-1) isolated during the first wave was neutralized by antibodies appearing at the end of the first viremic phase, but the virus (SHIVKU-1b) isolated during the second viremic phase was not neutralized by these antibodies. Inoculation of SHIVKU-1b into 4 pig-tailed macaques resulted in severe CD4 (+) T cell loss by 2 weeks postinoculation, and all 4 macaques died from AIDS at 23-34 weeks postinoculation. Because this virus had a neutralization-resistant phenotype, we sequenced the env gene and compared these sequences with those of the env gene of SHIVKU-1 and parental SHIV-4. With reference to SHIV-4, SHIVKU-1b had 18 and 6 consensus amino acid substitutions in the gp120 and gp41 regions of Env, respectively. These compared with 10 and 3 amino acid substitutions in the gp120 and gp41 regions of SHIVKU-1. Our data suggested that SHIVKU-1 and SHIVKU-1b probably evolved from a common ancestor but that SHIVKU-1b did not evolve from SHIVKU-1. A chimeric virus, SHIVKU-1bMC17, constructed with the consensus env from the SHIVKU-1b on a background of SHIV-4, confirmed that amino acid substitutions in Env were responsible for the neutralization-resistant phenotype. These results are consistent with the hypothesis that neutralizing antibodies induced by SHIVKU-1 in pig-tailed macaque resulted in the selection of a neutralization-resistant virus that was responsible for the second wave of viremia. Copyright 1999 Academic Press.

6/AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09813315 98245151 PMID: 9576954
CCR5 coreceptor utilization involves a highly conserved arginine residue of HIV type 1 gp120.
Wang W K; Dudek T; Zhao Y J; Brumblay H G; Essex M; Lee T H
Department of Immunology and Infectious Diseases, Harvard School of Public Health, 651 Huntington Avenue, Boston, MA 02115, USA.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) May 12 1998, 95 (10) p5740-5, ISSN 0027-8424 Journal Code: 7505876
Contract/Grant No.: CA-39805; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The seven-transmembrane CCR5 was recently found to double as a coreceptor for a genetically diverse family of human and nonhuman primate lentiviruses. Paradoxically, the main region of the envelope protein believed to be involved in CCR5 utilization was mapped to hypervariable region 3, or V3, of the envelope glycoprotein gp120. In this study, we addressed the question of whether functional convergence in CCR5

utilization is mediated by certain V3 residues that are highly conserved among HIV type 1 (HIV - 1), HIV type 2, and simian immunodeficiency virus. Site-directed mutagenesis carried out on three such V3 residues revealed that the Arg-298 of HIV - 1 gp120 has an important role in CCR5 utilization. In contrast, no effect was observed for the other residues we tested. The inability of Arg-298 mutants to use CCR5 was not attributed to global alteration of gp120 conformation. Neither the expression, processing, and incorporation of mutant envelope proteins into virions, nor CD4 binding were significantly affected by the mutations. This interpretation is further supported by the finding that alanine substitutions of five residues immediately adjacent to the arginine residue had no effect on CCR5 utilization. Taken together, our data strongly suggests that the highly conserved Arg-298 residue identified in the V3 of HIV - 1 has a significant role in CCR5 utilization, and may represent an unusually conserved target for future anti-viral designs.

6/AB/4 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

09140655 Genuine Article#: 371YH Number of References: 38
Title: Expression and coreceptor function of APJ for primate immunodeficiency viruses (ABSTRACT AVAILABLE)
Author(s): Puffer BA; Sharron M; Coughlan CM; Baribaud F; McManus CM; Lee B ; David J; Price K; Horuk R; Tsang M; Doms RW (REPRINT)
Corporate Source: UNIV PENN,DEPT PATHOL & LAB MED, 806 ABRAMSON BLDG, 34TH & CIV CTR BLVD/PHILADELPHIA//PA/19104 (REPRINT); UNIV PENN,DEPT PATHOL & LAB MED/PHILADELPHIA//PA/19104; BERIEX BIOSCI,/RICHMOND//CA/94804; R&D SYST,/MINNEAPOLIS//MN/55413
Journal: VIROLOGY, 2000, V276, N2 (OCT 25), P435-444
ISSN: 0042-6822 Publication date: 20001025
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495
Language: English Document Type: ARTICLE
Abstract: APJ is a seven transmembrane domain G-protein-coupled receptor that functions as a coreceptor for some primate immunodeficiency virus strains. The in vivo significance of APJ coreceptor function remains to be elucidated, however, due to the lack of an antibody that can be used to assess API expression, and because of the absence of an antibody or ligand that can block APJ coreceptor activity. Therefore, we produced a specific monoclonal antibody (MAb 856) to APJ and found that it detected this receptor in FAGS, immunofluorescence, and immunohistochemistry studies. MAb 856 also recognized API by Western blot, enabling us to determine that APJ is N-glycosylated. Using this antibody, we correlated APJ expression with coreceptor activity and found that APJ had coreceptor function even at low levels of expression. However, we found that API could not be detected by FAGS analysis on cell lines commonly used to propagate primate lentiviruses , nor was it expressed on human PBMC cultured under a variety of conditions. We also found that some viral envelope proteins could mediate fusion with APJ-positive, CD4 -negative cells, provided that CD4 was added in trans. These findings indicate that in some situations APJ use could render primary cell types susceptible to virus infection, although we have not found any evidence that this occurs. Finally, the peptide ligand for APJ, apelin-13, efficiently blocked APJ coreceptor activity. (C) 2000 Academic Press.

6/AB/5 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04766485 Genuine Article#: UF923 Number of References: 51
Title: LIVE ATTENUATED HIV AS A VACCINE FOR AIDS - PROS AND CONS (Abstract Available)
Author(s): RUPRECHT RM; BABA TW; LI A; AYEHUNIE S; HU YW; LISKA V; RASMUSSEN R; SHARMA PL
Corporate Source: DANA FARBER CANC INST,LAB VIRAL PATHOGENESIS/BOSTON//MA/02115; HARVARD UNIV,SCH MED,DEPT MED/BOSTON//MA/00000; TUFTS UNIV,SCH MED,DEPT NEWBORN MED/BOSTON//MA/02111; HARVARD UNIV,SCH MED,DEPT PATHOL/BOSTON//MA/02115 ; BETH ISRAEL HOSP/BOSTON//MA/02215
Journal: SEMINARS IN VIROLOGY, 1996, V7, N2 (APR), P147-155
ISSN: 1044-5773
Language: ENGLISH Document Type: ARTICLE
Abstract: Anti-HIV-1 vaccines must be safe and effective. In macaques, live attenuated simian immunodeficiency viruses have provided the best protection to date. Similar results were obtained earlier in murine leukemia virus systems in which protection correlated with cellular immunity but not with neutralizing antibodies. Attenuated primate lentiviruses tested thus far have been replication-impaired but may still harbor genetic determinants encoding virulence. Other safety issues concern insertional oncogenesis, genetic instability, vertical transmission and differential pathogenicity in adults and newborns, and viral persistence with possible reactivation during intercurrent illness. Long term safety studies are needed to assess the risks associated with live attenuated retrovirus vaccines. (C)1996 Academic Press Ltd

6/AB/6 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04752199 Genuine Article#: UE997 Number of References: 17
Title: SIMILARITY BETWEEN NEF OF PRIMATE LENTIVIRUSES AND P15E OF MURINE AND FELINE LEUKEMIA VIRUSES
Author(s): COLLETTE Y; DUTARTRE H; BENZIANE A; OLIVE D
Corporate Source: INSERM U119,UNITE THERAPEUTH EXPT & CANCEROL APPL,27 BLVD LEI ROURE/F-13009 MARSEILLE//FRANCE/
Journal: AIDS, 1996, V10, N4 (APR), P441-442
ISSN: 0269-9370
Language: ENGLISH Document Type: LETTER

6/AB/7 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04651979 Genuine Article#: UA363 Number of References: 83
Title: PHYSICAL AND FUNCTIONAL INTERACTION OF NEF WITH LCK - HIV-1 NEF-INDUCED T-CELL SIGNALING DEFECTS (Abstract Available)
Author(s): COLLETTE Y; DUTARTRE H; BENZIANE A; RAMOSMORALES F; BENAROUS R; HARRIS M; OLIVE D
Corporate Source: INSERM,U119,27 BLVD LEI ROURE/F-13009 MARSEILLE//FRANCE/; INSERM,U119/F-13009 MARSEILLE//FRANCE/; INST COCHIN GENET MOLEC,INSERM,U363/F-75014 PARIS//FRANCE/; INST COCHIN GENET MOLEC,INSERM,U332/F-75014 PARIS//FRANCE/; UNIV GLASGOW,DEPT VET PATHOL/GLASGOW G61 1QH/LANARK/SCOTLAND/
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 1996, V271, N11 (MAR 15), P 6333-6341
ISSN: 0021-9258

Language: ENGLISH Document Type: ARTICLE
Abstract: The nef gene is unique to the primate lentiviruses and encodes a cytoplasmic membrane-associated protein that affects T-cell signaling and is essential for both maintenance of a high virus load in vivo and for disease progression. Here we investigated the perturbation of cell signaling by Nef in T-cells and found that Nef interacts with the T-cell restricted Lck tyrosine kinase both in vitro and in vivo. The molecular basis for this interaction was analyzed. We show that cell-derived Nef is precipitated in a synergistic manner by the recombinant Src homology 2 (SH2) and SH3 domains from Lck. A functional proline-rich motif and the tyrosine phosphorylation of Nef were evidenced as likely participants in this interaction, The precipitation of Nef by the Lck recombinant proteins was specific, since neither Fyn, Csk, p85 phosphatidylinositol 3-kinase nor phospholipase C gamma SH2 domains coprecipitated Nef from T-cells, Finally, depressed Lck kinase activity resulted from the presence of Nef, both in vitro and in intact cells, and nef expression resulted in impairment of both proximal and distal Lck-mediated signaling events, These results provide a molecular basis for the Nef-induced T-cell signaling defect and its role in AIDS pathogenesis.

6/AB/8 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04485766 Genuine Article#: TG499 Number of References: 38
Title: PATHOGENESIS OF LYMPHOCYTE-TROPIC AND MACROPHAGE TROPIC SIVMAC INFECTION IN THE BRAIN (Abstract Available)
Author(s): ZHU GW; LIU ZQ; JOAG SV; PINSON DM; ADANY I; NARAYAN O; MCCLURE HM; STEPHENS EB
Corporate Source: UNIV KANSAS,MED CTR,DEPT MICROBIOL MOLEC GENET & IMMUNOL,3901 RAINBOW BLVD/KANSAS CITY//KS/66160; UNIV KANSAS,MED CTR,DEPT MICROBIOL MOLEC GENET & IMMUNOL/KANSAS CITY//KS/66160; EMORY UNIV,YERKES REG PRIMATE RES CTR/ATLANTA//GA/30322
Journal: JOURNAL OF NEUROVIROLOGY, 1995, V1, N1 (MAR), P78-91
ISSN: 1355-0284
Language: ENGLISH Document Type: ARTICLE
Abstract: SIV(mac)239 replicates productivity in activated CD4 + T lymphocytes, but inefficiently in macrophages from rhesus macrophages. Inoculation of the virus into animals results in an acute, highly productive burst of virus replication in activated T lymphocytes in lymphoid tissues and infected cells invade the central nervous system (CNS). This phase lasts a few weeks and is eventually followed by development of immunosuppression of different degrees of severity, opportunistic infections, and tumors related to the loss of T lymphocytes. On rare occasions, infected immunosuppressed animals develop encephalitis and/or interstitial pneumonia, syndromes that are associated with selection of mutant viruses that replicate efficiently in macrophages of these tissues. Usually, however, brains of animals dying with AIDS caused by SIV(mac)239 appear histologically normal. Is the brain infected with virus? We report here on a macaque dying with AIDS, a neuroinvasive tumor and interstitial pneumonia associated with macrophage-tropic virus. Except for focal infiltration of tumor cells, the brain was normal histologically. We examined the virus and viral DNA from different tissues and found that lymphocytes but not macrophages from lymph nodes and spleen yielded virus, whereas macrophages-but not lymphocytes from the lung produced virus. No virus was recovered from the brain but small amounts of viral p27 were present in the brain homogenate. Viral sequences were present in the brain as determined by PCR from tissue DNA. Comparison showed that the

viral sequences in the brain closely resembled those from the spleen. Presumably, the virus caused a minimally productive infection detectable by production of small amounts of p27, but was not accompanied by any histopathological changes. It is unclear why the macrophage-tropic virus in the lung failed to 'take-off' in the brain of this animal. To determine whether this virus had encephalitic potential, we inoculated the lung homogenate containing cell-free, macrophage tropic virus into a young pigtail macaque, a species known to be sensitive to primate lentiviral infections. This animal developed severe encephalitis 10 weeks later. Virus from the brain was very similar to the inoculum virus, proving its encephalitic potential. Possible reasons for the differences in neurovirulence of this virus between the two animals remain speculative.

6/AB/9 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04463778 Genuine Article#: TE732 Number of References: 45
Title: CHARACTERIZATION OF A CD4 -EXPRESSING MACAQUE CELL-LINE THAT CAN DETECT VIRUS AFTER A SINGLE REPLICATION CYCLE AND CAN BE INFECTED BY DIVERSE SIMIAN IMMUNODEFICIENCY VIRUS ISOLATES (Abstract Available)
Author(s): CHACKERIAN B; HAIGWOOD NL; OVERBAUGH J
Corporate Source: UNIV WASHINGTON,DEPT MICROBIOL,BOX 35742/SEATTLE//WA/98195; UNIV WASHINGTON,DEPT MICROBIOL/SEATTLE//WA/98195; BRISTOL MYERS SQUIBB PHARMACEUT RES INST/SEATTLE//WA/98121
Journal: VIROLOGY, 1995, V213, N2 (NOV 10), P386-394
ISSN: 0042-6822
Language: ENGLISH Document Type: ARTICLE
Abstract: Primate lentiviruses such as human immunodeficiency virus (HIV) and simian immunodeficiency virus (SIV) are phenotypically diverse, and virus isolates vary in cytopathicity, replication rate, and cell tropism. While all Virus isolates infect primary peripheral blood lymphocytes, only a subset of strains infect established CD4 -expressing T-cell lines. Here, we describe the development and characterization of a macaque cell line that can be infected by all of the strains of SIV that we have tested, including macrophage- and T-cell-tropic strains, primary and cell-line adapted strains, and SIVmac, SIVMne, and SIVsm isolates. The cells can be infected by strains or HIV type 2 (HIV-2) to varying degrees, but not by either cloned or primary isolates of HIV type 1 (HIV-1). This cell line is a derivative of a rhesus macaque mammary tumor cell line (CMMT) engineered to express human CD4 . For these studies, a CMMT- CD4 clone expressing an integrated copy of a truncated HIV-1 long terminal repeat fused to the beta-galactosidase gene (LTR-beta-gal) was established to allow detection of infectious SIV after a single round of replication. Here, we demonstrate the ability of the CMMT- CD4 -LTR-beta-gal cell line to rapidly and quantitatively detect infectious SIV. Using these cells to assay virus, we could readily measure neutralizing antibody activity in animals infected with different SIV isolates. Neutralizing activity was detected against the homologous virus and lower, but detectable, activity was measured against heterologous virus. Thus, this system, which is highly sensitive and can detect infection by all of the SIV isolates we tested, is a rapid method for detecting infectious virus and quantitating neutralizing antibody activity. (C) 1995 Academic Press, Inc.

6/AB/10 (Item 7 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04145772 Genuine Article#: RH854 Number of References: 54
Title: REPAIR AND EVOLUTION OF NEF IN-VIVO MODULATES SIMIAN IMMUNODEFICIENCY VIRUS VIRULENCE (Abstract Available)
Author(s): WHATMORE AM; COOK N; HALL GA; SHARPE S; RUD EW; CRANAGE MP
Corporate Source: PUBL HLTH LAB SERV,CTR APPL MICROBIOL & RES/SALISBURY SP4 0JG/WILTS/ENGLAND/; DEPT HLTH & WELF,BUR HIV AIDS,LAB CTR DIS CONTROL/OTTAWA/ON K1A 0L2/CANADA/
Journal: JOURNAL OF VIROLOGY, 1995, V69, N8 (AUG), P5117-5123
ISSN: 0022-538X
Language: ENGLISH Document Type: NOTE
Abstract: Experimental evidence from the simian immunodeficiency virus (SIV) model of AIDS has shown that the nef gene is critical in the pathogenesis of AIDS. Consequently, nef is of considerable interest in both antiviral drug and vaccine development. Preliminary findings in two rhesus macaques indicated that a deletion of only 12 bp found in the overlapping nef/3' long terminal repeat (LTR) region (9501 to 9512) of the SIVmacC8 molecular clone was associated with reduced virus isolation frequency. We show that this deletion can be repaired in vivo by a sequence duplication event and that sequence evolution continues until the predicted amino acid sequence of the repair is virtually indistinguishable from that of the virulent wild type. These changes occurred concomitantly with reversion to virulence, evidenced by a high virus isolation frequency and load, decline in anti-p27 antibody, substantial reduction in the CD4 /CD8 ratio, and development of opportunistic infections associated with AIDS. These findings clearly illustrate the capacity for repair of small attenuating deletions in primate lentiviruses and also strongly suggest that the region from 9501 to 9512 in the SIV nef/3' LTR region is of biological relevance. In addition, the ability of attenuated virus to revert to virulence raises fundamental questions regarding the nature of superinfection immunity.

6/AB/11 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03847185 Genuine Article#: QL683 Number of References: 32
Title: PROGRESSION TO AIDS IN THE ABSENCE OF A GENE FOR VPR OR VPX (Abstract Available)
Author(s): GIBBS JS; LACKNER AA; LANG SM; SIMON MA; SEHGAL PK; DANIEL MD; DESROSIERS RC
Corporate Source: HARVARD UNIV,NEW ENGLAND REG PRIMATE RES CTR,SCH MED,1 PINE HILL DR,BOX 9102/SOUTHBOROUGH//MA/01772; HARVARD UNIV,NEW ENGLAND REG PRIMATE RES CTR,SCH MED/SOUTHBOROUGH//MA/01772
Journal: JOURNAL OF VIROLOGY, 1995, V69, N4 (APR), P2378-2383
ISSN: 0022-538X
Language: ENGLISH Document Type: ARTICLE
Abstract: Rhesus monkeys (Macaca mulatta) were experimentally infected with strains of simian immunodeficiency virus (SIV) derived from SIV(mac)239 lacking vpr, vpx, or both vpr and vpx genes, These auxiliary genes are not required for virus replication in cultured cells but are consistently conserved within the SIVmac/human immunodeficiency virus type 2/SIVsm group of primate lentiviruses. All four rhesus monkeys infected with the vpr deletion mutant showed an early spike in plasma antigenemia, maintained high virus burdens, exhibited declines in CD4 (+) lymphocyte concentrations, and had significant changes in lymph node morphology, and two have died to date with AIDS, The behavior of

the vpr deletion mutant was indistinguishable from that of the parental, wild-type virus, Rhesus monkeys infected with the vpx deletion mutant showed lower levels of plasma antigenemia, lower virus burdens, and delayed declines in CD4 (+) lymphocyte concentrations but nonetheless progressed with AIDS to a terminal stage, The vpr + vpx double mutant was severely attenuated, with much lower virus burdens and no evidence of disease progression, These and other results indicate that vpr provides only a slight facilitating advantage for wild-type SIVmac replication in vivo. Thus, progression to AIDS and death can occur in the absence of a gene for vpr or vpx.

6/AB/12 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03847143 Genuine Article#: QL683 Number of References: 48
Title: MOLECULAR AND BIOLOGICAL ANALYSES OF QUASI-SPECIES DURING EVOLUTION OF A VIRULENT SIMIAN IMMUNODEFICIENCY VIRUS, SIVSMMPBJ14 (Abstract Available)
Author(s): TAO BL; FULTZ PN
Corporate Source: UNIV ALABAMA,DEPT MICROBIOL,845 19TH ST S,BBRB 511/BIRMINGHAM//AL/35294; UNIV ALABAMA,DEPT MICROBIOL/BIRMINGHAM//AL/35294; UNIV ALABAMA,CTR AIDS RES/BIRMINGHAM//AL/35294
Journal: JOURNAL OF VIROLOGY, 1995, V69, N4 (APR), P2031-2037
ISSN: 0022-538X
Language: ENGLISH Document Type: ARTICLE
Abstract: A prototypic simian immunodeficiency virus (SIVsmm9), isolated from a naturally infected sooty mangabey (Cercocebus atys), was passaged in vivo in a pig-tailed macaque (Macaca nemestrina) having the identifier PBj. When PBj died of a typical AIDS-like syndrome 14 months after infection, the virus isolated from its tissues was subsequently shown to differ from SIVsmm9 genetically and biologically. Most notably, this isolate, SIVsmmPBj14 (SIV-PBj14), is the most virulent primate lentivirus known: it induces acute disease and death within 6 to 10 days after intravenous inoculation into pig-tailed macaques. Between the time of infection with SIVsmm9 and isolation of SIV-PBj14, isolates were obtained periodically from peripheral blood mononuclear cells of PBj. To establish the temporal relationship between evolution of new biologic properties and fixation of specific mutations in the virus population, these sequential SIV-PBj isolates were characterized for unique properties of SIV-PBj14 that appeared to correlate with acute lethal disease. These properties included the ability to replicate in quiescent macaque peripheral blood mononuclear cells, to activate and induce proliferation of CD4 (+) and CD8(+) cells, and to exhibit cytopathicity for mangabey CD4 (+) lymphocytes. Consistent with earlier studies, a major change in biologic properties occurred between 6 (SIV-PBj6) and 10 (SIV-PBj10) months, with the SIV-PBj8 quasispecies exhibiting properties of bath earlier and later isolates. Multiple biologic clones derived from the 6-, 8-, and 10-month isolates also exhibited diverse phenotypes. For example, one SIV-PBj10 biologic clone resembled SIVsmm9 phenotypically, whereas three other biologic clones resembled SIV-PBj14. To evaluate genetic changes, proviral DNA of the biologic clones generated from SIV-PBj6, -PBj8, and -PBj10 was amplified by PCR in the U3 enhancer portion of the long terminal repeats (LTR) and the V1 region of env, where the greatest nucleotide diversity between SIVsmm9 and SIV-PBj14 resided. Nucleotide sequence data indicated that all biologically cloned viruses are distinct and that insertions/duplications of 3 to 27 nucleotides (in multiples of three) had accumulated stepwise in the env V1 region, beginning with

SIV-PBj8. In addition, one of four SIV-PBj8 biologic clones had a 22-bp duplication in the LTR which is characteristic of SIV-PBj14. When virus mixtures containing different proportions of two SIV-PBj10 biologic clones with opposite phenotypes were tested, the SIV-PBj14 phenotype was clearly dominant, since mixtures with as few as 10% of the viruses being SIV-PBj14-like exhibited all the properties of the lethal isolate. The results suggest that neither the duplication of the NF-KB binding site in the LTR nor the duplications/insertions in env V1 (nor a combination of both mutations) were sufficient to confer the SIV-PBj14 biologic phenotype. However, because some of the unique SIV-PBj14 properties segregate, further analysis of biologically and molecularly cloned viruses derived from these sequential isolates should lead to the identification of viral determinants for specific traits.

6/AB/13 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03547413 Genuine Article#: PL736 Number of References: 97
Title: GENETIC DIVERSITY OF HUMAN-IMMUNODEFICIENCY-VIRUS TYPE-2 - EVIDENCE FOR DISTINCT SEQUENCE SUBTYPES WITH DIFFERENCES IN VIRUS BIOLOGY (Abstract Available)
Author(s): GAO F; YUE L; ROBERTSON DL; HILL SC; HUI HX; BIGGAR RJ; NEEQUAYE AE; WHELAN TM; HO DD; SHAW GM; SHARP PM; HAHN BH
Corporate Source: UNIV ALABAMA,DEPT MED,701 S 19TH ST,LHRB 613/BIRMINGHAM//AL/35294; UNIV ALABAMA,DEPT MED/BIRMINGHAM//AL/35294; UNIV ALABAMA,DEPT MICROBIOL/BIRMINGHAM//AL/35294; UNIV NOTTINGHAM,QUEENS MED CTR,DEPT GENET/NOTTINGHAM NG7 2UH//ENGLAND/; NCI,VIRAL EPIDEMIOL BRANCH/BETHESDA//MD/00000; UNIV GHANA,SCH MED,DEPT MED/ACCRA//GHANA/; SEROL INC/ATLANTA//GA/00000; NYU,SCH MED,AARON DIAMOND AIDS RES CTR/NEW YORK//NY/00000
Journal: JOURNAL OF VIROLOGY, 1994, V68, N11 (NOV), P7433-7447
ISSN: 0022-538X
Language: ENGLISH Document Type: ARTICLE
Abstract: The virulence properties of human immunodeficiency virus type 2 (HIV-2) are known to vary significantly and to range from relative attenuation in certain individuals to high level pathogenicity in others. These differences in clinical manifestations may, at least in part, be determined by genetic differences among infecting virus strains. Evaluation of the full spectrum of HIV-2 genetic diversity is thus a necessary first step towards understanding its molecular epidemiology, natural history of infection, and biological diversity. In this study, we have used nested PCR techniques to amplify viral sequences from the DNA of uncultured peripheral blood mononuclear cells from 12 patients with HIV-2 seroreactivity. Sequence analysis of four nonoverlapping genomic regions allowed a comprehensive analysis of HIV-2 phylogeny. The results revealed (i) the existence of five distinct and roughly equidistant evolutionary lineages of HIV-2 which, by analogy with HIV-1, have been termed sequence subtypes A to E; (ii) evidence for a mosaic HIV-2 genome, indicating that coinfection with genetically divergent strains and recombination can occur in HIV-2-infected individuals; and (iii) evidence supporting the conclusion that some of the HIV-2 subtypes may have arisen from independent introductions of genetically diverse sooty mangabey viruses into the human population. Importantly, only a subset of HIV-2 strains replicated in culture: all subtype A viruses grew to high titers, but attempts to isolate representatives of subtypes C, D, and E, as well as the majority of subtype B viruses, remained unsuccessful. Infection with all five viral subtypes was detectable by commercially available

serological (Western immunoblot) assays, despite intersubtype sequence differences of up to 25% in the gag, pol, and env regions. These results indicate that the genetic and biological diversity of HIV-2 is far greater than previously appreciated and suggest that there may be subtype-specific differences in virus biology. Systematic natural history studies are needed to determine whether this heterogeneity has clinical relevance and whether the various HIV-2 subtypes differ in their in vivo pathogenicity.

6/AB/14 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03501583 Genuine Article#: PJ186 Number of References: 69
Title: ANTIGENIC VARIATION OF PRIMATE LENTIVIRUSES IN HUMANS AND EXPERIMENTALLY INFECTED MACAQUES
Author(s): FENYO EM
Corporate Source: KAROLINSKA INST,MTC,DEPT MICROBIOL & TUMORBIOL,BOX 280/S-17177 STOCKHOLM//SWEDEN/
Journal: IMMUNOLOGICAL REVIEWS, 1994, V140, AUG (AUG), P131-146
ISSN: 0105-2896
Language: ENGLISH Document Type: REVIEW

6/AB/15 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

02490763 Genuine Article#: LE916 Number of References: 53
Title: B-CELL ANTIGENIC SITES IN THE ENVELOPE PROTEINS OF PRIMATE LENTIVIRUSES AND THEIR ROLE IN VACCINE DEVELOPMENT
Author(s): NORRBY E; MATTHEWS T
Corporate Source: KAROLINSKA INST,SBL,SCH MED,DEPT VIROL/S-10521 STOCKHOLM//SWEDEN/; DUKE UNIV,MED CTR/DURHAM//NC/27710
Journal: AIDS, 1993, V7, S1, PS127-S133
ISSN: 0269-9370
Language: ENGLISH Document Type: ARTICLE

6/AB/16 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

07343014 EMBASE No: 1998251873
G protein-coupled receptors in HIV and SIV entry: New perspectives on lentivirus-host interactions and on the utility of animal models
Unutmaz D.; KewalRamani V.N.; Littman D.R.
D. Unutmaz, Howard Hughes Medical Institute, New York University Medical Center, 540 First Avenue, New York, NY 10016 United States
Seminars in Immunology (SEMIN. IMMUNOL.) (United Kingdom) 1998, 10/3 (225-236)
CODEN: SEIME ISSN: 1044-5323
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 97

Entry of primate lentiviruses into target cells has recently been shown to depend upon the interaction of the viral envelope glycoprotein with CD4 and one or more members of the G protein-coupled receptor (GPCR) family of transmembrane proteins. In vivo, the transmission of HIV-1

infection generally requires viral strains that utilise chemokine receptor CCR5, and these strains prevail during the early course of infection. Strains isolated later, in the course of progression to immunodeficiency, are often CXCR4-tropic or are dual tropic for both chemokine receptors . SIV isolates also use CCR5 but are only rarely specific for CXCR4. Instead, SIVs use two orphan members of the GPCR family, named Bonzo/STRL33/TYMSTR and BOB/GPR15. Strains of HIV-2, which are closely related to the SIVs, also often utilise CXCR4, CCR5, BOB and/or Bonzo. Additional GPCR family members have also been shown to be utilised by various strains of HIV and SIV, albeit less efficiently and less frequently. Here we discuss the potential relationship between receptor specificity and viral pathogenesis as well as efforts to develop animal model systems to study the mechanism of disease progression.

6/AB/17 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01774531 SUPPLIER NUMBER: 20850106 (USE FORMAT 7 OR 9 FOR FULL TEXT)
CCR5 Coreceptor Utilization Involves a Highly Conserved Arginine Residue of HIV Type 1 gp120.
AIDS Weekly Plus, pNA(1)
June 29,
1998
PUBLICATION FORMAT: Newsletter ISSN: 1069-1456 LANGUAGE: English
RECORD TYPE: Fulltext TARGET AUDIENCE: Professional; Trade
WORD COUNT: 361 LINE COUNT: 00032

6/AB/18 (Item 2 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01611515 SUPPLIER NUMBER: 17901053 (USE FORMAT 7 OR 9 FOR FULL TEXT)
The emerging genetic diversity of HIV: the importance of global surveillance for diagnostics, research, and prevention.
Hu, Dale J.; Dondero, Timothy J.; Rayfield, Mark A.; George, J. Richard; Schochetman, Gerald; Jaffe, Harold W.; Luo, Chi-Cheng; Kalish, Marcia L.; Weniger, Bruce G.; Pau, Chou-Pong; Schable, Charles A.; Curran, James W.
JAMA, The Journal of the American Medical Association, v275, n3, p210(7)
Jan 17,
1996
PUBLICATION FORMAT: Magazine/Journal ISSN: 0098-7484 LANGUAGE: English
RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 7601 LINE COUNT: 00641

ABSTRACT: Increased surveillance of HIV variants is necessary to determine their impact on human populations. Two types of HIV have been reported. HIV-1 is the virus predominant in the US and other countries, while HIV-2 has been reported from Western Africa. Each virus can mutate into subtypes. A single individual could contain several different, but related variants. HIV-1 has eight subtypes, designated A through H. The B subtype of HIV-1 is the predominant subtype in the US, and most of the diagnostic tests and vaccines have been based on subtype B. A worldwide surveillance system is needed to monitor the appearance and spread of different variants. Molecular techniques such as the polymerase chain reaction should improve the detection of variants. Research is needed to determine if different variants have different clinical effects.
AUTHOR ABSTRACT: The discovery of highly divergent strains of human immunodeficiency virus (HIV) not reliably detected by a number of commonly

used diagnostic tests has underscored the need for effective surveillance to track HIV variants and to direct research and prevention activities. Pathogens such as HIV that mutate extensively present significant challenges to effective monitoring of pathogens and to disease control. To date, relatively few systematic large-scale attempts have been made to characterize and sequence HIV isolates. For most of the world, including the United States, information on the distribution of HIV strains among different population groups is limited. We describe herein the implications resulting from the rapid evolution of HIV and the need for systematic surveillance integrated with laboratory science and applied research. General surveillance guidelines are provided to assist in identifying population groups for screening, in applying descriptive epidemiology and systematic sampling, and in developing and evaluating efficient laboratory testing algorithms. Timely reporting and dissemination of data is also an important element of surveillance efforts. Ultimately, the success of a global surveillance network depends on collaboration and on coordination of clinical, laboratory, and epidemiologic efforts. (JAMA. 1996;275:210-216)

6/AB/19 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

012531589
WPI Acc No: 1999-337695/199928
Related WPI Acc No: 1999-327359; 1999-337640; 1999-337709
XRAM Acc No: C99-099299
Modified gp120 lentiviral protein with increased stability
Patent Assignee: DANA FARBER CANCER INST INC (DAND); UNIV COLUMBIA NEW YORK (UYCO)
Inventor: FARZAN M; HENDRICKSON W A; KWONG P D; SODROSKI J G; WYATT R T
Number of Countries: 022 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9924465	A1	19990520	WO 98US24001	A	19981110	199928	B
AU 9913963	A	19990531	AU 9913963	A	19981110	199941	

Priority Applications (No Type Date): US 98100764 A 19980618; US 97966932 A 19971110; US 97966987 A 19971110; US 97967148 A 19971110; US 97967403 A 19971110; US 97967708 A 19971110; US 97976741 A 19971124; US 9889580 P 19980617; US 9889581 P 19980617; US 98100521 A 19980618; US 98100529 A 19980618; US 98100631 A 19980618; US 98100762 A 19980618; US 98100763 A 19980618
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9924465	A1	E	72	C07K-014/16	
Designated States (National): AU CA JP US					
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
AU 9913963	A				Based on patent WO 9924465

Abstract (Basic): WO 9924465 A1
Abstract (Basic):
NOVELTY - Modified gp120 polypeptide (I) comprising portions of at least two conserved regions of an envelope protein from a primate lentivirus , is new.
DETAILED DESCRIPTION - Modified gp120 polypeptide (I) includes, relative to wild-type gp120 glycoprotein, at least one of the changes:
(i) introduction of disulfide bonds;
(ii) filling a cavity with hydrophobic amino acid (aa);
(iii) introduction of a proline (Pro) at a defined turn structure;

and/or

(iv) increased hydrophobicity across the interface between gp120 domains.

(I) maintains the overall three-dimensional structure of a discontinuous conserved epitope of wild-type gp120.

ACTIVITY - Antiviral; Immunostimulant.

MECHANISM OF ACTION - Vaccine.

USE - (I), or nucleic acids encoding them, are used in vaccines to elicit a protective immune response against human immune deficiency virus. Antibodies raised against (I) can be used to minimize risk of HIV infection, e.g. by topical application before intercourse, or administered systemically to inhibit viral replication in blood and tissue.

ADVANTAGE - The specified modifications produce a polypeptide that has increased stability; generates a range of antibodies to conserved epitopes and/or has increased immunogenicity for broadly neutralizing epitopes.

pp; 72 DwgNo 0/4

6/AB/20 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

012521253
WPI Acc No: 1999-327359/199927
Related WPI Acc No: 1999-337640; 1999-337695; 1999-337709
XRAM Acc No: C99-096941
New glycosylated modified envelope polypeptides useful in vaccines against HIV infection
Patent Assignee: DANA FARBER CANCER INST INC (DAND); UNIV COLUMBIA NEW YORK (UYCO)
Inventor: HENDRICKSON W A; KWONG P D; SODROSKI J G; WYATT R T
Number of Countries: 022 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9924464	A1	19990520	WO 98US23998	A	19981110	199927	B
AU 9913962	A	19990531	AU 9913962	A	19981110	199941	

Priority Applications (No Type Date): US 98100764 A 19980618; US 97966932 A 19971110; US 97966987 A 19971110; US 97967403 A 19971110; US 97967708 A 19971110; US 97976148 A 19971110; US 97976741 A 19971124; US 9889580 P 19980617; US 9889581 P 19980617; US 98100521 A 19980618; US 98100529 A 19980618; US 98100631 A 19980618; US 98100762 A 19980618; US 98100763 A 19980618

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9924464	A1	E	68	C07K-014/16	
	Designated States (National): AU CA JP US				
	Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE				
AU 9913962	A				Based on patent WO 9924464

Abstract (Basic): WO 9924464 A1
Abstract (Basic):

NOVELTY - New modified gp120 polypeptides comprise portions of at least two conserved regions of an envelope protein of a primate lentivirus having modified glycosylation sites and maintain the overall 3-dimensional structure of a discontinuous conserved epitope of the wild-type gp120.

DETAILED DESCRIPTION - The modified gp120 polypeptides that

maintain the overall 3-dimensional structure of a discontinuous conserved epitope of the wild-type gp120 comprise portions of at least two conserved regions of an envelope protein of a primate lentivirus where:

(a) at least two of the glycosylation sites proximal to the CD4 binding site or chemokine receptor binding site have been altered, where the alteration prevents glycosylation at the sites; or

(b) glycosylation sites distal to the CD4 binding site or chemokine receptor binding site have been derivatized with a molecular adjuvant.

ACTIVITY - Anti-HIV.

MECHANISM OF ACTION - Vaccine.

USE - The modified HIV-1 glycoproteins are useful for raising antibodies and are useful in vaccines against HIV infection. The antibodies can be included in ointments, foams or creams that can be used during sex. Alternatively they can be used prior to or just after sexual contact such as intercourse.

ADVANTAGE - The modified gp120 proteins have a structure approximating the conformational discontinuous epitopes of a HIV-1 envelope glycoprotein , that as a result of modifications of glycosylation sites on that structure raise a greater range of antibodies to conserved epitopes and/or have enhanced immunogenicity for broadly neutralizing epitopes. The modifications allow an increased accessibility to conserved gp120 epitopes that are related to the CD4 and chemokine receptor binding sites, and that are normally partially masked by a large variable loop structure. Inclusion of a pan-reactive T cell helper epitope can improve the immunogenicity of weakly immunogenic conserved or glycosylated, variable gp120 regions.

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